

F.G.

Neutralization against HIV-1 primary isolates from clades A, B, C and E after last DNA immunization

04.4.			Clade B	В			Clade C		Clade A	Cla	Clade E
Study groups	Animal no.	ADA	SF162	Bal	JRCSF	TVI	DU151	S007	DJ263	CM235	CM244
Mono-valent	R101	0.0	34.2	6.01	21.2	0.0	0.0	40.0	0.0	0.0	0:0
	R102	0.0	37.9	11.3	12.1	0.0	0.9	0.0	0.0	0.0	0.0
	R104	16.0	76.0	15.0	34.0	43.6	0.0	13.8	44.9	0.0	0.0
	R105	4.0	55.0	15.0	46.0	27.1	8.2	0.0	4.0	0.0	0.0
	R106	16.9	9.65	4.0	30.0	31.6	17.6	11.3	39.0	0.0	2.4
	R107	1.8	47.9	5.8	21.5	22.5	0.0	9.0	21.3	0.0	2.4
	R109	0.0	38.6	0.0	18.9	14.2	33.8	0.0	32.0	0.0	29.9
	R110	8.9	46.6	0.0	0.0	16.9	0.0	21.1	12.2	0.0	19.7
Poly-valent	R301	0.0	71.8	17.9	45.6	0.0	0.0	0.0	0.0	0.0	0.0
	R302	0.0	42.1	0.0	16.3	14.0	0.0	39.0	0.0	0.0	0.0
	R801	0.0	63.5	5.2	40.7	26.0	1.0	0.0	3.0	0.0	0.0
	R802	0.0	34.8	0.0	0.0	31.0	0.0	10.0	28.0	0.0	0.0
Control	R001	0.0	0.0	0.0	0.0	0.0	0.0	4.0	0.0	0.0	0.9
Positive											
antibodies	Concentration		•								
HIVIG	10 mg/ml	8.96	99.1	6.86	8.86	98.1	4.96	1001	98.4	95.3	98.1
			95.6	84.1	83.1	19.0	58.6	6.69	75.0	29.3	35.2
2F5		74.9	92.9	86.7	93.2	76.5	29.0	39.2	27.9	91.2	\$6.4
	5 µg/ml		67.8	52.6	76.4	29.0	16.6	17.5	10.8	65.2	61.4
2G12	50 µg/ml	32.7	59.2	75.9	77.9	28.2	5.5	2.3	1.06	4.7	0.0
	5 µg/ml	20.3	43.6	53.3	57.9	15.7	16.0	0.6	77.0	0.0	0.9

FIG. 2

Neutralization against HIV-1 primary isolates from clades A, B, C and E after the first protein boost

Thurster concentration	· Carlowin V		Clade B	e B			Clade C		Clade A	Clade E	le E
Study groups	Amma no.	ADA	SF162	Bal	JRCSF	TVI	DU151	2002	D1263	CM235	CM244
Mono-valent	R101	0.0	80.4	58.9	70.4	21.0	0.0	47.0	24.0	0.0	0.0
	R102	0.0	74.6	63.9	57.0	14.0	0:0	0.0	0.0	0.0	0.0
	R104	31.5	95.0	0.18	0.69	59.7	0:0	5.4	57.7	0.0	0.0
	R105	0.9	46.5	88.0	84.0	81.2	0.0	0.0	41.5	0.0	0.0
	R106	10.8	47.4	31.1	30.0	20.4	15.4	27.5	42.7	0.0	0.0
	R107	2.7	54.0	0.0	6.2	39.5	0.0	7.0	16.7	0.0	26.2
	R109	13.0	35.1	0.0	19.7	40.3	1.3	0.0	44.4	0.0	8.5
	R110	10.5	31.9	0.0	0.0	34.8	4.9	34.3	36.5	0.0	28.4
Poly-valent	R301	11.5	93.6	93.6	90.5	0.68	23.0	0.0	14.0	0.0	0.0
	R302	0.0	91.5	79.6	84.2	87.0	33.0	54.0	55.0	0.0	27.0
	R801	0.0	84.8	9.19	73.9	0.89	23.0	31.0	36.0	0.0	0.0
	R802	0.0	73.0	13.5	41.4	74.0	0.0	13.0	65.0	0.0	0.0
Control	R001	0.0	33.5	0.2	24.1	0.0	0.0	36.0	0.0	0.0	6.0
Positive											
antibodies	Concentration										
HIVIG	10 mg/ml	8.90	1'66	6'86	98.8	98.1	96.4	1001	48,4	95.3	98.1
	l mg/ml	44.6	95.6	%.I	83.1	19	58.6	6.69	75	29.3	35.2
2F5	50 µg/ml	74.9	92.9	86.7	93.2	76.5	29	39.2	27.9	91.2	X6.4
	5 µg/ml	43.4	67.8	52.6	76.4	29	9:91	17.5	10.8	65.2	61.4
2G12	50 µg/ml	32.7	59.2	75.9	77.9	28.2	5.5	2.3	7.9	4.7	0
	5 ug/ml	20.2	74	, , ,	0			,	!	(•

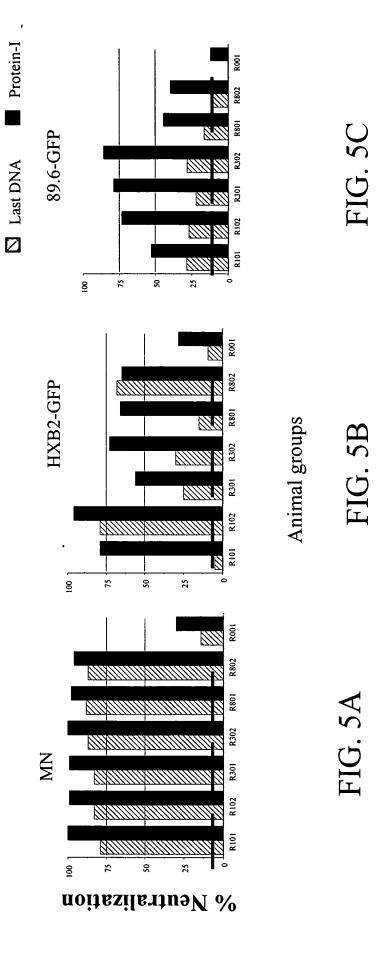
FIG. 3

Neutralization against HIV-1 primary isolates from clades A, B, C and E after the second protein boost

4. 4.	. 0 = 10 = 1	Clade B				Clade C			Clade A	Clade E	le E
Study groups	Anunai no.	ADA	SF162	Bal	JRCSF	TV1	DU151	S007	DJ263	CM235	CM244
Mono-valent	R101	0.0	89.5	70.0	6.79	0.0	0.0	0.0	22.0	0.0	27.7
	R102	1.0	77.3	9.95	49.4	52.8	0:0	0.0	56.4	0.0	17.0
	R104	33.5	94.0	87.0	0.67	80.0	22.8	33.0	65.7	0.0	0.0
	R105	37.0	92.0	84.0	84.0	81.9	34.9	0.0	49.5	0.0	0.0
	R106	35.1	92.6	82.1	80.7	79.9	54.1	62.5	79.8	25.5	33.4
	R107	26.1	92.1	76.6	82.3	0.06	0.0	8.99	68.5	0.0	45.3
	R109	37.2	88.9	44.9	48.5	76.8	0.0	3.4	68.2	0.0	0.0
	R110	11.3	26.3	0.0	52.6	77.6	43.7	59.1	70.0	0.0	28.4
Poly-valent	R301	24.0	94.7	81.2	82.6	79.2	8.7	39.0	70.2	10.9	33.4
	R302	13.0	93.2	75.2	67.1	47.3	0:0	44.0	64.0	10.1	23.7
	R801	24.0	91.4	74.9	7.67	72.9	0.0	42.4	62.5	3.3	32.5
	R802	29.0	89.3	69.5	73.8	83.8	1.2	3.7	7.67	15.2	37.6
Control	R001	0.0	40.6	23.7	35.4	50.1	00	. 0	22.0	0.0	0.0
Positive											
antibodies	Concentration										
HIVIG	10 mg/ml	8.96	1.66	6.86	8.86	98.1	96.4	100.1	98.4	95.3	98.1
	1 mg/ml	44.6	9.56	84.1	83.1	19.0	58.6	6.69	75.0	29.3	35.2
2F5	50 µg/ml	74.9	92.9	86.7	93.2	76.5	29.0	39.2	27.9	91.2	86.4
	5 μg/ml	43.4	8.79	52.6	76.4	29.0	16.6	17.5	10.8	65.2	61.4
2G12	50 µg/ml	32.7	59.2	75.9	6.77	28.2	5.5	2.3	90.1	4.7	0.0
	5 µg/ml	20.3	43.6	53.3	57.9	15.7	16.0	0.6	77.0	0.0	0.9

FIG. 4

Neutralization of HIV-1 clade B viruses



Anti-Env IgG responses after DNA priming measured by ELISA

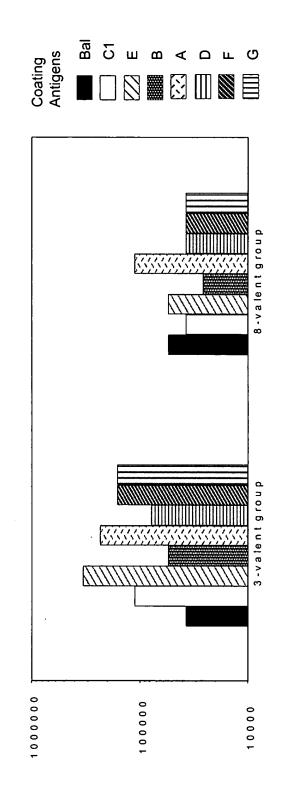
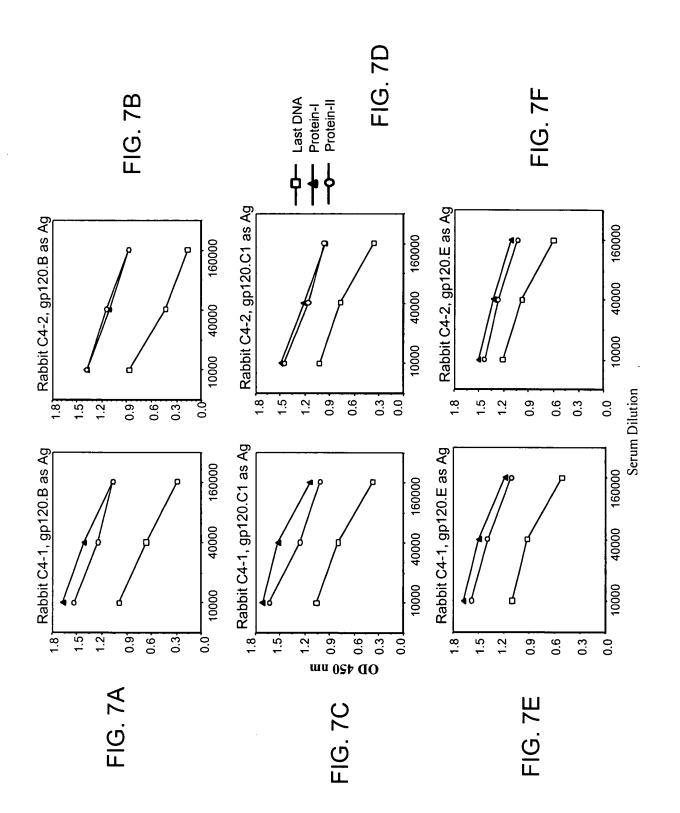
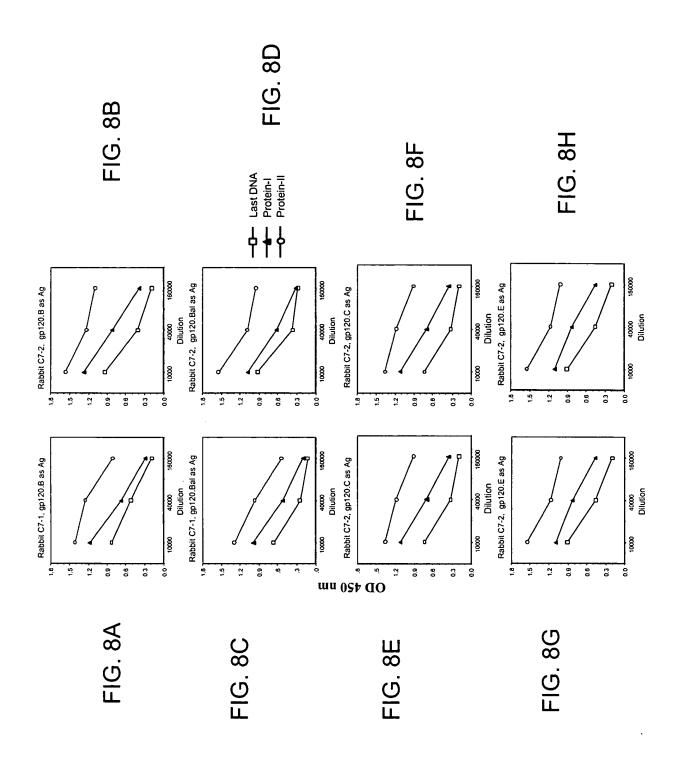
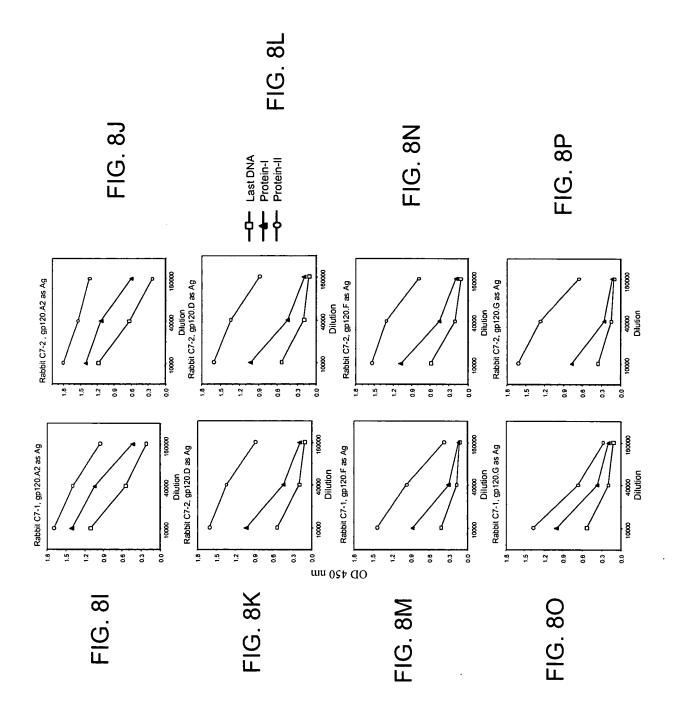


FIG. 6







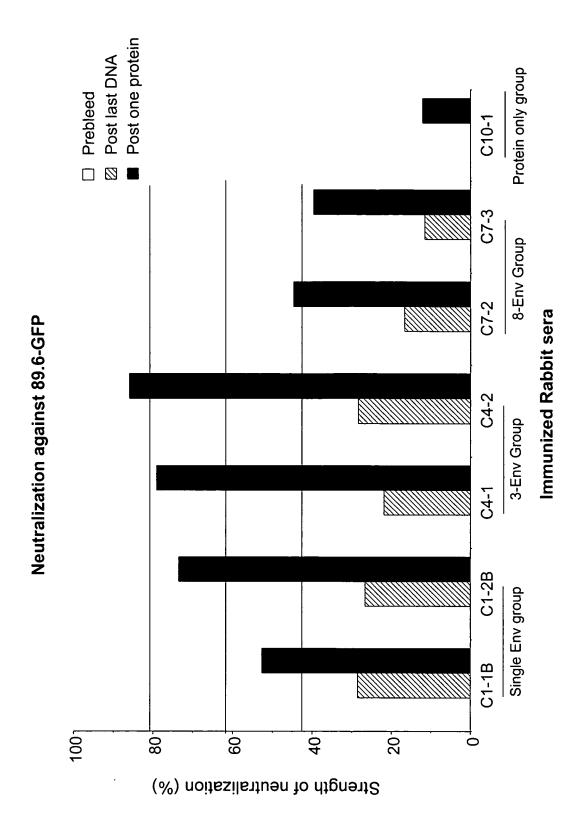


FIG. 9

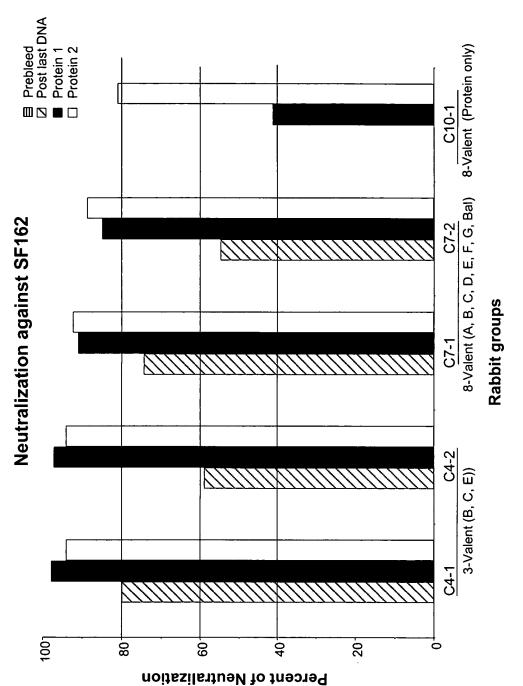
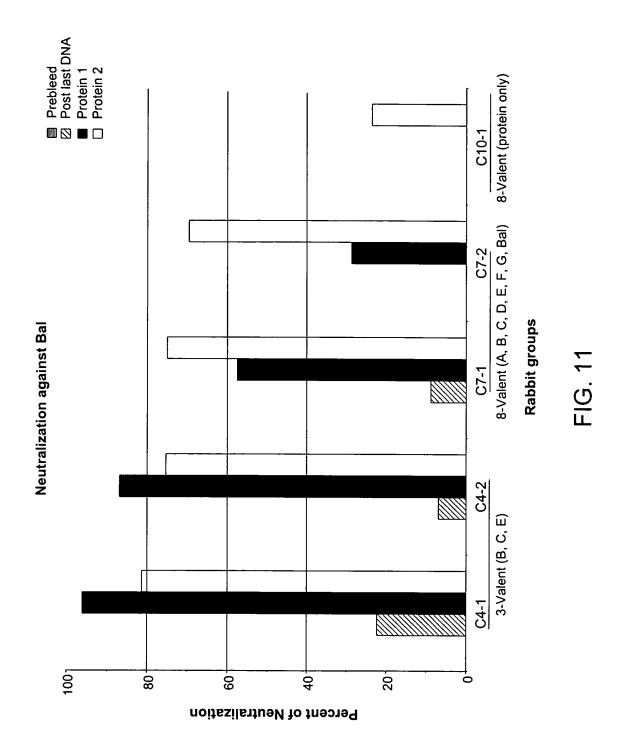


FIG. 10



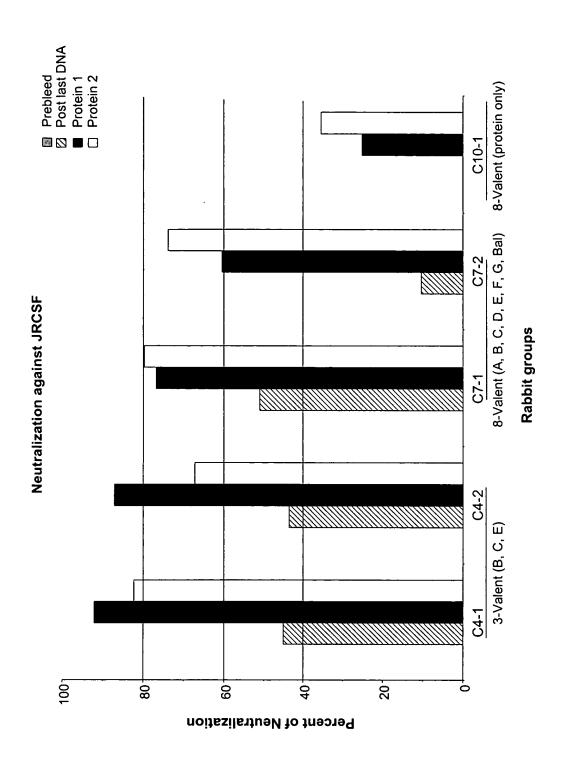


FIG. 12

Percent of Meutralization

Probleed
Description
Protein 1
Protein 2

Neutralization against TV1 (clade C)

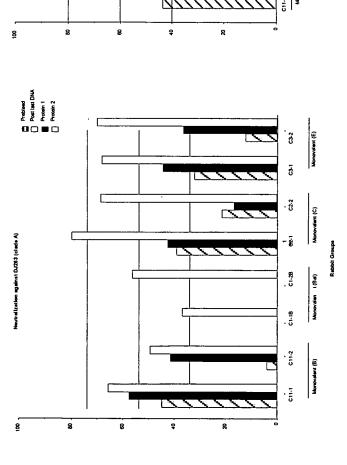
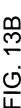


FIG. 13A



8 2222

CG-1 Manovalent (C)

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C1-28

C1-18 C

245

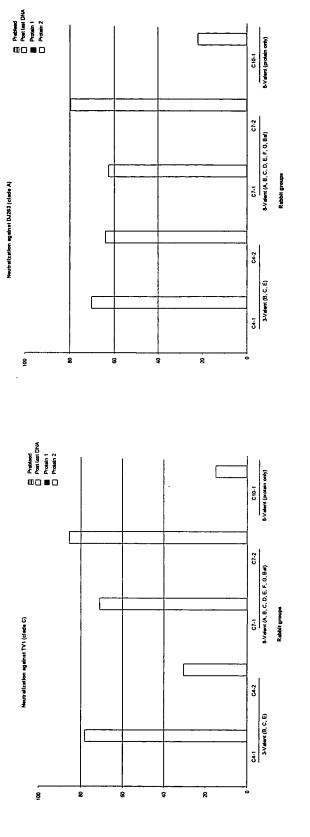


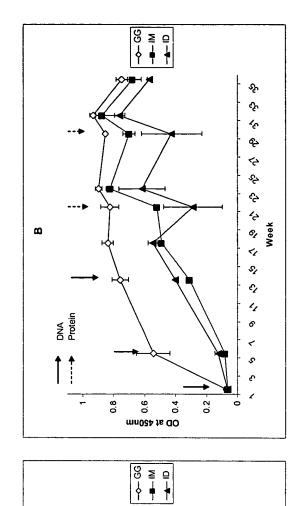
FIG. 13D

FIG. 13C

+a

TITEMI OF	78 SLØDÇSLKPCVKITPLCVTLNCT <u>obr</u> -nytngez-notnytssskringeggerkncsfritn or gkkvokbyllfykldi 78 SLØDQSLKPCVKITPLCVTLNCT <u>NOR-notnorg</u> -notnytssskrindeggerkncsfrittsbrokk <u>vokb</u> rld <u>y</u> 81 SLØDQSLKPCVKLTPLCVTLNCTBVA-NOTNÖN-SBVNNTBRNNNSNAGGONKNCSFRITTELRDKKVONTLYKLDI 78 SLØDQSLKPCVKITPLCVTLÄCTNBRENGTNÖTNGNRTUNGSRAGGNURDE ENRNCSFINTTELRDKKOKVALFYKLDI	150 VÕINNÕNNSSNÄYRLINCNTSÄLTQACPKVÕFEPIPIÄYCAPAGYAILKCNDKÄFNGTGÄCÄNVSTVQCTHGIRP 154 超直通N	225 VVSTQLLLNGSLABEEVÄIRSENÄTNNÄKÄIIVQLNEÄVÄINCTRPNNNTRKSÄRIGPGQEFYÄTGDIIGDIRQAHCNYS 227 VVSTQLLLNGSLABEEVÄIRSÄNÄÄÄNAKÄIIVQLNESVEINCTRPNNNTRKSIÄIGPGRÄFYÄTGÄIIGDIRQAHCNYS 227 VVSTQLLLNGSLABEEVÄIRSÄNISÄÄNAKTIIVQLNESVÄNUCTRPNNNTRKSIÄIGPGRÄFYÄTGÄIIGDIRQAHCNYS 238 VVSTQLLNGSLABEEÄÄÄIRSENITNNÄKTIIVÄLNRSÄELÄCÄRPNNNTRÄSIRIGPGOÄFYÄTGDIIGDIRQAHCNÄS 227 VVSTQLLNGSLABEEÄÄÄISENITNNÄKTIIVÄLNRSVEIÄCTRPÄÄNTRÄSIRIGPGOÄFYÄTGDIÄGDIRÄÄÄÄGÄÄÄ	305 <u>659</u> 0NRPLHOVGOLREWINNITIERNISSGOLEITTHSFNCGGEFFYCNTSGLFNSNWRENGERSWA-BROZITLPCR 307 RYKONDTLWROVIKLREGEGNKTIVERSGOBEITTHSFNCGGEFFYCNSTOLFNSTWWOGG-BSNNTVERNITLPCR 307 RTKONETLROVERLREGEBNKTIVERSGOBEITTHSFNCGGEFFYCNSTKLFNSTWWGG-BSNNT-GEBEITLPCR 318 RTWWERTLROVENKLREHERWKIDFRESSGOLEITTHSFNCGGEFFYCNTSGLFSWWYGGS-GENNT-BOURITLPCR 307 ETKONERILKOVRIKERFERWKIIDFRESSGOLEITTHSFNCGGEFFYCUTGLFSWWYGGS-GENNT-BOURITLPCR	383 IKQIINWWQBVGGABYAPPIBGZIRCESNITGLDILTRDGGSNYSENESGIFRPGGGDMRDNWRSELYKYKVVRIEPLG 387 IKQIINWWQEVGRAMYAPPIRGGIRCESNITGLLTRDGGESSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSS	459 NAPTRAKRRVVQ (SEQ ID NO:17) 463 NAPTRAKRRVVQ (SEQ ID NO:18) 463 IAPTRAKRRVVQ (SEQ ID NO:20) 473 IAPTRAKRRVVERM (SEQ ID NO:20) 458 IAPTRAKRVVQ (SEQ ID NO:21)	
A gp120 Ba-L gp120 B715 gp120 Czm gp120 E gp120	Ba-1, gp120 B715 gp120 Czm gp120 E gp120	A gp120 Ba-L gp120 B715 gp120 Czm gp120 E gp120	A gp120 Ba-L gp120 B715 gp120 Czm gp120 E gp120	A gp120 Ba-L gp120 B715 gp120 Czm gp120 E gpi20	A gp120 Ba-L gp120 B715 gp120 C2m gp120 E gp120	A gp120 Ba-L gp120 B715 gp120 Czm gp120 E gp120	

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DNA Protein

0.8

mn024 1s QO 0 0 0 4

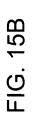
FIG. 15A

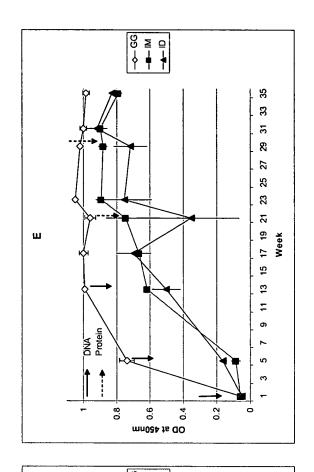
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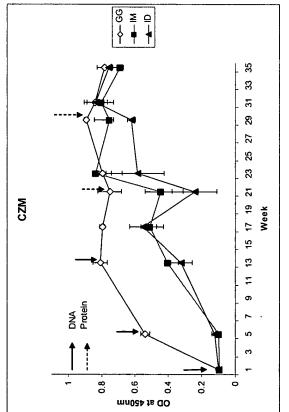


FIG. 15D

FIG. 15C

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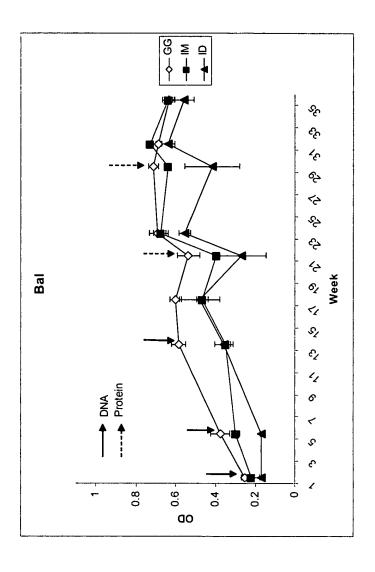
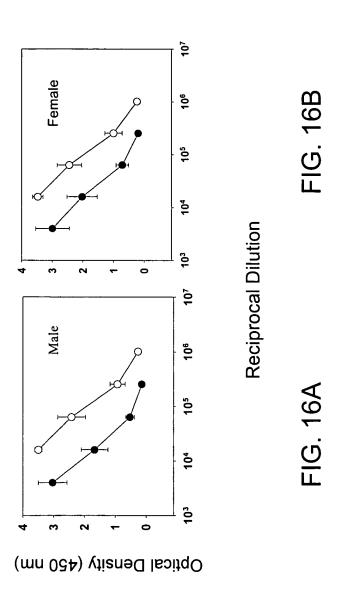


FIG. 15E

Anti-gp120 response in rabbits immunized intramuscularly with DP6-001



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Anti-gp120 response in rabbits immunized intradermally with DP6-001

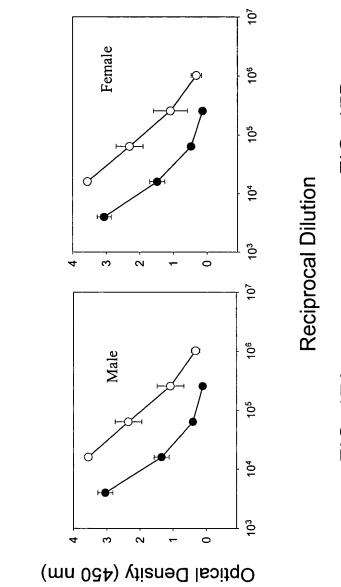
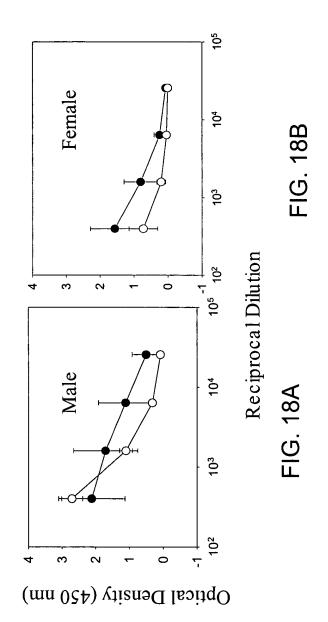


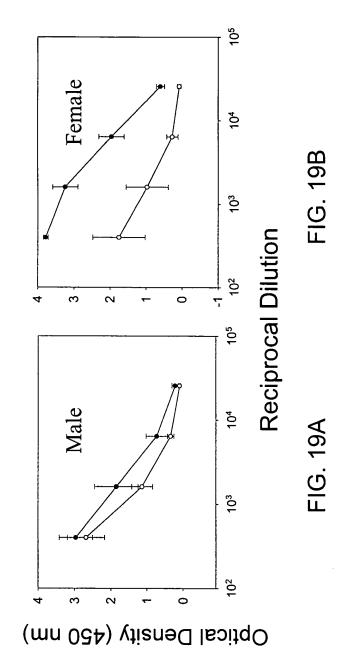
FIG. 17B

Anti-gag response in rabbits immunized intramuscularly with DP6-001



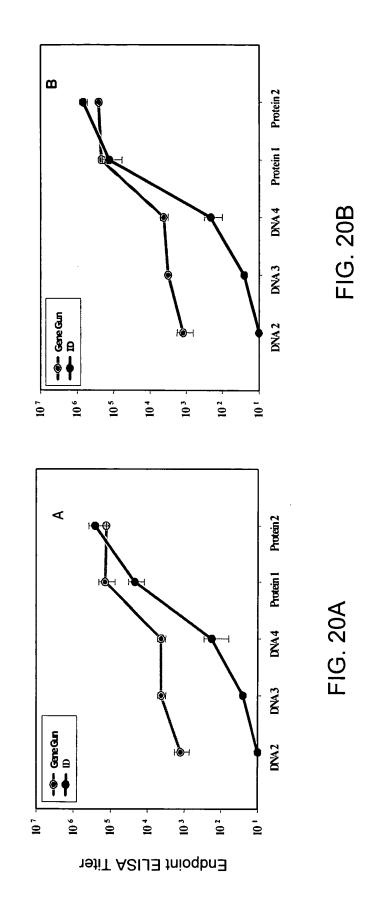
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Anti-gag response in rabbits immunized intradermally with DP6-001

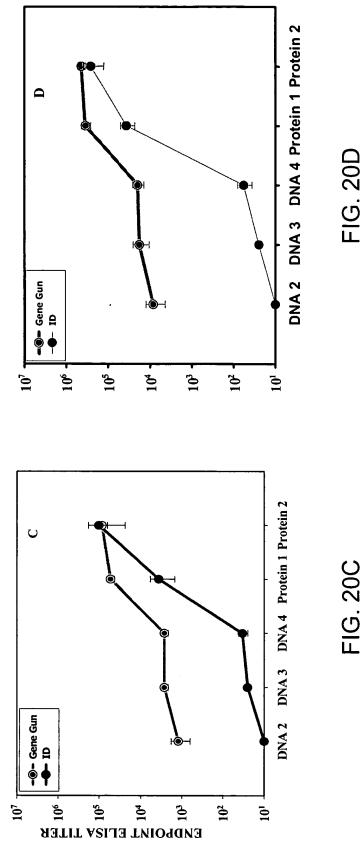


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Antibody titers in macaques immunized with polyvalent DNA and gp120 protein



Antibody titers in macaques immunized with polyvalent DNA and gp120 protein



Antibody titers in macaques immunized with polyvalent DNA and gp120 protein

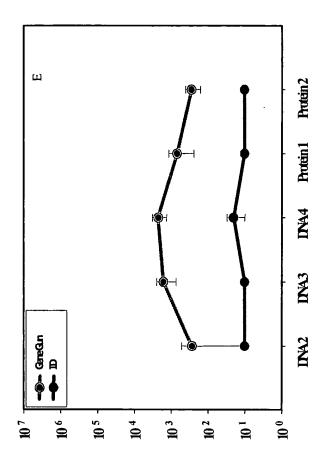
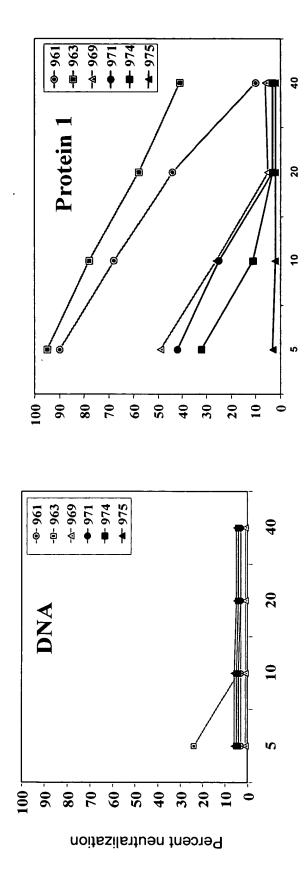


FIG. 20E



Reciprocal serum dilution FIG. 21A

FIG. 21B

Percent neutralization

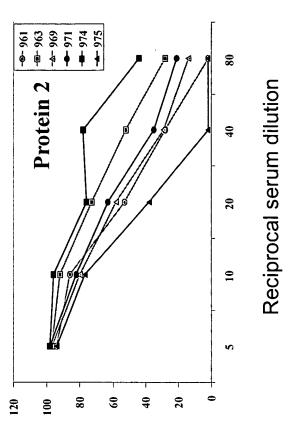
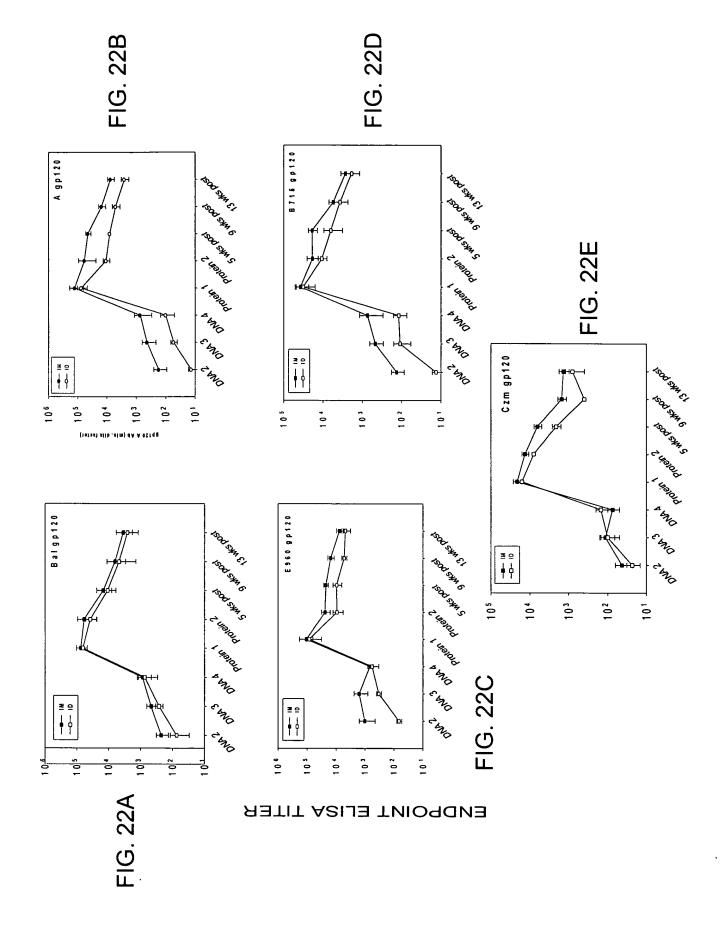
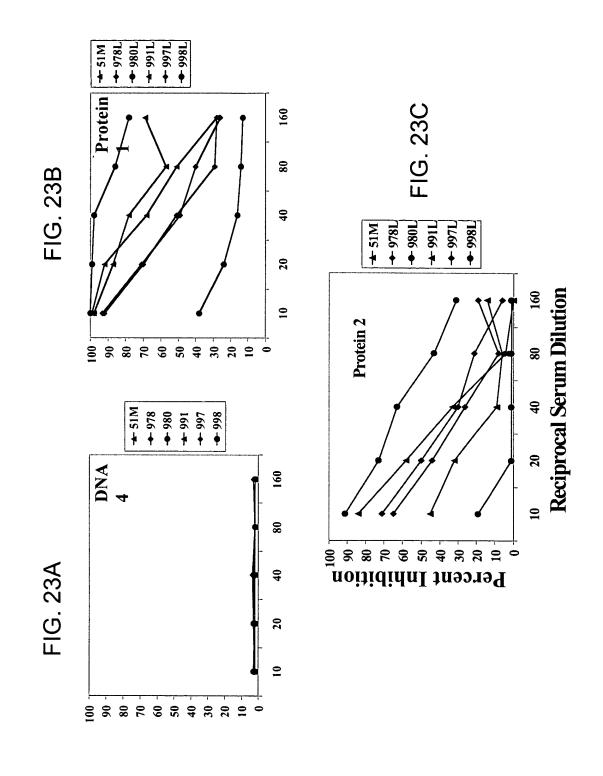
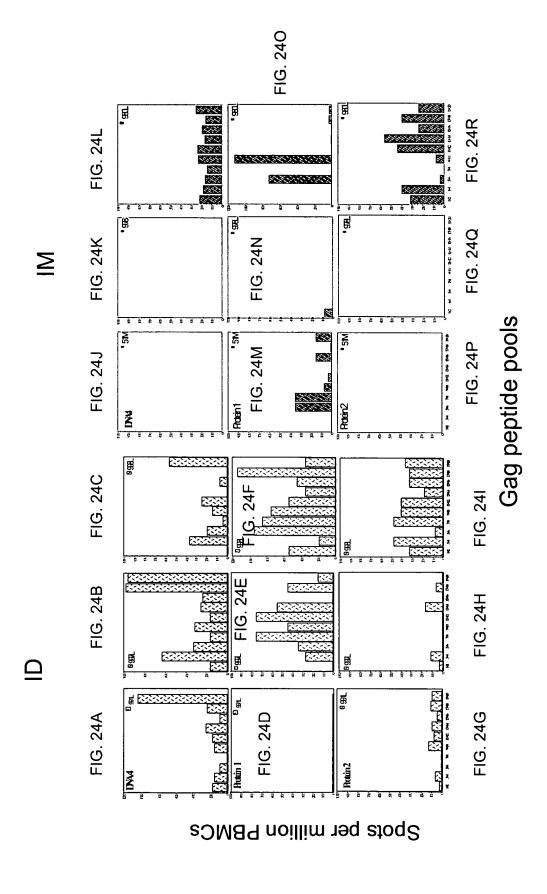
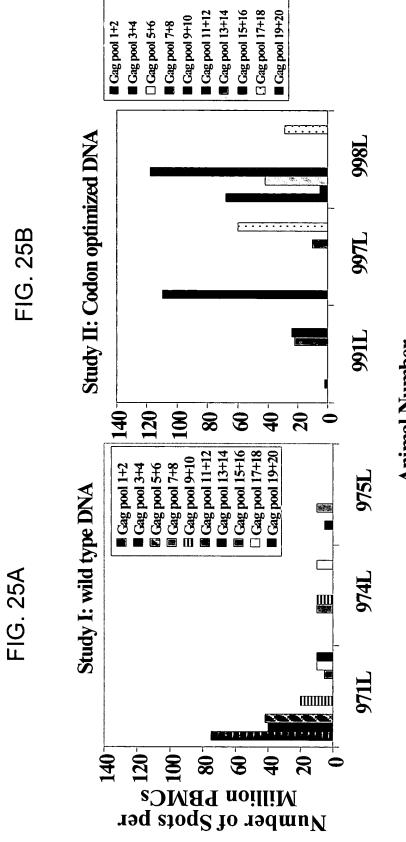


FIG. 21C









Animal Number

51M 978 991 991 998 51M 978 0 980 0 991 0 997 Protein 1 Protein | Pool 4 FIG. 26B Pool 3 Pool 3 Pool 2 Pool 2 Envelope Peptide Pool Pool 1 Pool 1 DNA 4 Pool 4 DNA 4 Pool 4 FIG. 26A Pool 3 Pool 3 FIG. 26C Pool 2 Pool 2 Pool 1 Pool 1 Ba-L 90 85 80 70 70 65 60 50 50 40 35 885 880 775 770 660 660 850 35 30

Spots per million PBMC

Wild type Gag.Czm DNA sequence:

ATCCAGTGCATGCAGGGCCTATTGCACCAGGCCAAATGAGAGAACCAAGGGGAAGTGATATAGCAGGAACTACTAGTACCC CAGAAGGCTGTAAACAAATAATGAAACAGCTACAACCAGCTCTTCAGACAGGAACGGAGGAACTTAGATCATTATACAACA <u> AAAATGCAAACCCAGATTGCAAGACCATTTTAAAAGCATTAGGACCAGGGGCTACATTAGAAGAAATGATGACAGCATGTC</u> A GCAGAGAGCTTCAGGTTCGAGGAGACAACCCCCGCTCCGAAGCAGGAGTCGAAAGACAGGGAAGCCTTAACTTCCCTCAA TAAATAAAATAGTAAGAATGTATAGCCCTGTCAGCATTTTGGACATAAAACAAGGGCCAAAGGAACCCTTTAGAGACTATG A A G G A G G G G G G C C A A G C C A A G C A A G C A A G G C T G A G G C C A A T G A C C A A C A A C A T A C T G A T G A G C C A A C A A C A T A C T A C T G A T G A G C A A C A A C A T A C T A C T A C T G A T G A G C A A A C A C A A C A C A A C A C A A C A C A A C A C A A C A C A A C AACGCTATATGATAAAACACCTAGTATGGGCAAGCAGGGAGCTGGAAAGATTTGCGCTTAACCCTGGCCTTTTAGAAACAT CAGTAGCAACTCTCTATTGTGTACATGAAGGGGTAGAGGTACGAGACACCCAAGGAAGCCTTAGACAGGATAGAGGAAGAA IACAGTGGGGGGACATCAAGCAGCCATGCAAATGTTAAAAGATACTATCAATGAGGAGGCTGCAGAATGGGATAGATTAC TCCAAGAACAGATAGCATGGATGACAAGTAATCCCCCTATTCCAGTGGGAGACATCTATAAAAGATGGATAAATTCTGGGGT ITITITAGGGAAAATITGGCCTTCCCACAAGGGAAGGCCAGGGAATTTCCTTCAGAACAGGCCAGAGACAACAGCCAACA GCAGAATCTCCAAGGGCAAATGGTACACCAGAAACTATCACCTAGAACTTTGAATGCATGGGTAAAAGTAATAGAAGAAA <u> ATGGGTGCGAGAGCGTCAATATTAAGAGGGGGAAAATTAGATAAATGGGAAAAATTAGGCTAAGGCCAGGGGGAAAGA</u> ATCACTCTTTGGCAGCGACCCCTTGTCTCAATAA (SEQ ID NO:5)

Codon optimized Gag.Czm DNA sequence:

CAAAGCAAGAGTGCTCGCCGAGGCCATGAGCCAGACCAACAGCGTGAATATCCTGATGCAGAAGAGC GCCTGAACAAGATCGTGAGAATGTACAGCCCCGTGAGCATCCTGGACATCAAGGACCTAAGGA CTCTGGGACCCGGCCCACACTGGAAGAGATGATGACAGCATGCCAGGGCGTCGGAGGACCAAGCCA GCACAGAGCGGCAAGCAAACTTCCTCGGAAAGATCTGGCCAAGGCCACAAGGGAAGACCCGGCAATTT GAGGGCGTGGAAGTGCGGGACACCAAGGAGGCCCTGGACCGGATCGAGGAAGAGAGAAAAAAGATC <u> AAGGACACCATCAACGAGGAAGCTGCCGAGTGGGACAGACTGCATCCAGTCCACGCCGGACCCATCG</u> GATCGCTTGGATGACCAGCAACCCCCCTATCCCCGTCGGCGACATCTACAAGCGGTGGATCATCCTGG A A GAA CTGGA TGA CCGA CA CA CTGCTGGTC CA GAA CGC CAA CCC CGA CTGC A GGA CCATCCTGAA GG CACTGAATCCTGGCCTCCTGGAGACCAGCGAAGGATGCAAACAGATCATGAAGCAGCTCCAACCAGC AGGTGATCGAAGAGAAGGCCTTCAGCCCTGAAGTGATCCCCATGTTCACAGCTCTGAGCGAAGGCGC ATGGGAGCCAGAGCCAGCATCCTGAGAGGAGGCAAACTGGACAAGTGGGAGAAGATTAGACTGCGG GTCCAGAACCTCCAGGGCCAGATGGTGCACCAGAAGCTGAGCCCTCGGACACTGAACGCCTGGGTCA CACTCCTCAGGACCTGAACACCATGCTGAACACCGTGGGAGGCCACCAAGCTGCAATGCAGATGCTG GCCCTTCAGAGACTACGTCGACCGGTTCTTTAAGACTCTGAGAGCCGAGCAGCCAGGAGGTG retecadacedeceteadaacteadaagectetatacaacacegtegecetetactecte CAGCAAA AGATCCAGCAGAAGACCCAACAGGCCGCTGATGGAAAGGTGAGGCAGAACTACCCCATC CTCCTGGCCAGATGCGGGAACCTAGAGGAAGCGATATCGCTGGCACTACCTCCACCCTGCAAGAGCA CCTGCAGAACAGACCTGAGCCCACCGCCCCACCTGCTGAGAGCTTCCGGTTCGAAGAGACCACACCC GCCCCCAAGCAGGAGACAAGGACAGAGCACTGACCAGCCTGAAGAGCCTGTTCGGCAGCGAT CCCTGAGCCAGTGA (SEQ ID NO:6)

Wild type gp120.Bal DNA sequence:

ATCAGTITATGGGATCAAAGCCTAAAGCCATGTGTAAAATTAACTCCACTCTGTGTTACTTTAAATTGCACTGATTT CCTGTCCAAAGATATCCTTTGAGCCAATTCCCATACATTATTGTGCCCCGGCTGGTTTTGCGATTCTAAAGTGTAAA GATAAGAAGTTCAATGGAAAAGGACCATGTTCAAATGTCAGCACAGTACAA TGTACACATGGGATTAGGCCAGTA FGCCCCTCCCATCAGAGGACAAATTAGATGTTCATCAAATATTACAGGGCTGCTATTAACAAGAGATGGTGGTCCA AAGCATATGATACAGAGGTACATAATGTTTGGGCCACACATGCCTGTGTACCCACAGACCCCAAGAAG TTGTAACCTTAGTAGAGCAAAATGGAATGACACTTTAAATAAGATAGTTATAAAATTAAAGAGAACAATTTGGGAA 3AGGCAAACAAGACCGAGGTCTTCAGACCTGGAGGAGGAGATATGAGGGACAATTGGAGAAGTGAATTATATAA TTGTGGGTCACAGTCTATTATGGGGTACCTGTGTGGAAAGAAGCAACCACCACCACTCTATTTTGTGCATCAGATGCTA GTATCAACTCAACTGCTGTTAAATGGCAGTCTAGCAGAAGAAGAGGTAGTAATTAGATCCGAAAATTTCGCGGAC FAAAACAATAGTCTTTAAGCATTCCTCAGGAGGGGACCCAGAAATTGTGACGCACAGTTTTAATTGTGGAGGGGA IAGAATTGGAAAATGTGACAGAAAATTTTAACATGTGGAAAAATAACATGGTAGAACAGATGCATGAGGATATA ATTITITCTACTGTAATTCAACACACTGTTTAATAGTACTTGGAATGTTACTGAAGAGTCAAATAACACTGTAGAA AATAACACATCACACTCCCATGCAGAATAAAACAAATTATAAACATGTGGCAGAAAGTAGGAAGAGCAATGTA

-1G. 29

Codon optimized gp120.Bal DNA sequence:

<u> AGCAGCCGCGCCATGGTGGGCGGCGGCGAGATGAAGAACTGCAGCTTCAACATCACCACCAACATCCGCGGCAAGGTGCAGAAGG</u> GTGATCACCCAGGCCTGCCCCAAGGTGAGCTTCGAGCCCATCCCATCCACTACTGCGCCCCCGCCGCCGGCTTCGCCATCCTGAAGTGC GCCTTCTACACCACCGGCGAGATCATCGGCGACATCCGCCAGGCCCACTGCAACCTGAGCCGCGCGCAAGTGGAACGACGCCTGAA
 ACCCACAGCTTCAATTGCGGCGGCGAGTTCTTCTACTGCAACAGCACCCAGCTGTTCAACAGCACCTGGAACGTGACCGAGGAGAG
 CAACAAGACCGAGGTGTTCCGCCCCGGCGGCGGCGACATGCGCGACAACTGGCGCAGCGAGCTGTACAAGGTACAAGGTGGAAG CTGTGGGTGACCGTGTACTACGGCGTGCCCGTGTGGAAGGAGGCCACCACCACCACTGTTCTGCGCCAGCGACCGCAAGGCCTACGA <u> SAGAACTTCAACATGTGGAAGAACAACATGGTGGAGCAGATGCACGAGGACATCATCATCAGCCTGTGGGACCAGAGCCTGAAGCCCT</u> AGTACGCCCTGTTCTACAAGCTGGACATCGCCCCATCGACAACAACAGCAACAACGGCTACCGCTGATCAGCTGCAACAACAGC AAGGACAAGAAGTTCAACGGCAAGGGCCCCTGCACCAACGTGAGCACCGTGCAGTGCACCCACGGCATCCGCCCGTGGTGAGCA CACCGAGGTGCACAACGTGTGGGCCACCCACGCCTGCGTGCCACCGACCCCAACCCCCAGGAGGTGGAGCTGAAGAACGTGACC CAAGATCGTGATCAAGCTGCGCGAGCAGTTCGGCAACAAGACCATCGTGTTCAAGCACAGGCGGCGGCGGCGGCGACCCCGAGATCGTG ATGTACGCCCCCCCACCATCCGCGGCCAGATCCGCTGCAGTTCGAACATCACCGGCCTGCTGCTGACCCGCGGCGGCCGGGCCCGAGGA CCCAGCTGCTGCTGAACGGCAGCCTGGCCGAGGAGGAGGTGGTGATCCGCAGCGCCAACTTCGCCGACAACGCCAAGGTGATCAT ATCGAGCCCCTGGGCGTGGCCCCCCACCAAGGCCCAAGCGCCGCGTGGTGGAGTAA (SEQ ID NO:8)

Wild type gp120.B DNA sequence:

<u> FAAAGCATATGATACAGAGGTACATAATGTTTGGGCCACACATGCCTGTGTACCCACAGACCCCGATCCACAG</u> IGCTCAGCTTTAATTGTGGAGGGGAATTTTTCTACTGTAATTCAACAAAACTGTTTAATAGTACTTGGAATGGTA CTATTAACAAGAGATGGTGAACAGTAACGAGACCAATACCACCGAGATCTTCAGACCTGGGGGGAGAATA <u> ACCAATCTGAGGAATGATACTAATACCACGAGGAATGCTACTAATACCACGAGTAGTGAGACAATGATGAGGGG</u> <u> IGAAGGACAATTGGAGAAGTGAATTATATATATATAAAGTAGTAAGAATTGAACCATTAGGAATAGCACCCAC</u> ITCTAAAGTGTAAAGATAAGAAGTTCAATGGAACAGGACCATGTACAAATGTCAGCACAGTACAATGCACACA AGAAGTAGGAAAAGCAATGTATGCCCCTCCCATCAGAGGACAAATTAGATGCTCATCAAATATTACAGGACTG ITGTGGGTCACAGTCTATTATGGGGTACCTGTGTGGAAAGAAGCAACACCACCCTCTATTTTGTGCATCAGATGC AAGTAGAATTGGAAAATGTGACAGAAATTTTAACATGTGGAAAAATAACATGGTAGAACAGATGCATGAGG FITTATAAACTTGATGTAGTACCAATAGAAAATGATACTACTAGCTATAGGTTGATAAGTTGTAATACCTCAG | FCCTTACACAGGCCTGCCCAAAGGTATCCTTTGAGCCAATTCCCATACATTTTTGTGCCCCGGCTGGTTTTGCAA IGGAATTAAGCCAGTAGTATCAACTCCAACTGCTGTTAAATGGCAGTCTAGCAGAAGAAGAGGGTAGTAATTAGG CTGAGTCAAATAACACAGGAGATGACCCAATCGTACTCCCATGCAGAATAAAACAAGTTATAAACATGTGGCA 4TATAATTAGTTTATGGGATCAAAGCCTAAAGCCATGTGTAAAATTAACCCCACTCTGTGTTACTCTAAATTGC
 ACCCAACAACAATACAAAAAGTATACATATAGGACCAGGCAGAGCATTTTATACAACAGGAGAAATAAT
 CAGGGCAAAGAGAAGAGTGGTGGAGTAA (SEQ ID NO:9)

Codon optimized gp120.B DNA sequence:

GTTTGCCCTTTTCTATAAACTTGATGTGGTGCCTATCGAGAATGACACTACTAGCTACAGGCTGATCAGCTGCACACCACCAGCGTCCTG AGAAGTTCAACGGCACCGGTCCTTGTACCAATGTCAGCACCGTACAATGCACCCACGGCATTAAGCCCGTGGTGAGCACTCAGCTGC FIGCTGAACGGCAGCCTGGCCGAGGAAGAGGTGGTGATTCGCTCCGCCAACCTCTGACAATGCTAAGACCATAATCGTGCAGCTGA CTTCAGGCCTGGGGGCGCCAACATGAAGGACAATTGGAGGAGCGAGTTATACAAATATAAGGTGGTGAGGATTGAGCCTCTGGGTA ACACAGGCCTGCCCCAAGGTGTCCTTCGAGCCAATTCCCATCCACTTTTGTGCCCCGGCTGGTTTCGCCATTCTAAAGTGCAAGGATA a ccedcea gatcateegeega catca egeca egecca cteta a cctta gea ega caa a gtega a cga ega ctetga a ga ga tegtea t 3GTCAGATTAGGTGCAGCAGCATATTACCGGCCTGCTACTGACCCGCGACGGCGGTAACAGCAACGAGCAACAACACACCACGAGAT <u>AAACTTCAACATGTGGAAGAATAACATGGTGGAGCAGATGCATGAGGATATCATTAGCCTGTGGGACCAGAGCCTAAAAGCCCTGCG</u>
 ACTGCGGTGGGGAGTTCTACTGTAACTCAACCAAGCTGTTTAATAGCACTTGGAACGGCACTGAGTCTAACAACACCGGTGATG
 A CCGA GGTGCA CAA TGTGTGGGCCA CCCA CGCCTGTGTGCCCA CCGA CCCCGA CCCTCA GGA GGTGGA GCTGGA GAA CGTGA CCGA ACGAGTCTGTGCAGATGAACTGCACGAGGCCCAACAACAATACCAGGAAGAGTATCCATATCGGTCCCGGCAGGGCATTCTATACC A C C C C A T C G T G C C A T G C A G C A G C A G G T G A T C A A C A T G T G G C A A G G C C A T G T A T G C C C T C C A T G C C A T G T C A G G C C A T G T A T G C C C T C C A T G T C A G G C A T G T A T G C C C T C C A T G T C A G G C A T G T A T G C C C T C C A T G T A T G C C C T C C A T G T A T G C C C T C A T G T A T G C C C T C A T G T A T G C C A T G T A T G C C A T G T A T G C C A T G T A T G C C A T G T A T G C C A T G T A T G C C A T G T A T G C C A T G T A T G C C A T G T A T G C C C T C C A T G T A T G C C A T G T A T G C C C T C C A T G T A T G C C A T G T A T G C C A T G T A T G C C A T G T A T G C C A T G T A T G C C A T G T A T G C C A T G T A T G C C A T G T A T G C C A T G T A T G C C A T G T A T CTGTGGGTGACCGTCTACTATGGGGTGCCTGTGTGGAAGGAGGCCAACACACCCTCTGTTCTGCGCTTCTGACGCTAAGGCCTACGAT rcgcccccaccagggccaagaggagggtggtgcagtaa (SEQ ID NO:10)

Wild type gp120.Czm DNA sequence:

IAGTITTGGGAAATGTAACAGAAATTTTAACATGTGGAAAAATGACATGGTGGATCAGATGCATGAGGATATAA GAAAAATTGCTCTTCAACATAACCACAGAACTAAAAGATAAGAAAAAGAATGTGTATGCACTTTTTATAAACTT GATATAGTATCACTTAATGAGACTGACGACTCTGAGACTGGCAACTCTAGTAAATATTATAATAAATTGTA IACAGATGGTACACCCATCACACTCCCATGCAGAATAAGACAAATTATAAATATGTGGCAGGAAGTAGGACGAGC ITGTGGGTCACAGTCTATTATGGGGTACCTGTGTGGAAAGAAGCAAAAACTACTCTATTCTGTGCATCAGATGCTA AATCATATGAGAAAGAAGTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAACCCAAGAAA **AATTAAGAGAACACTTCCCTAATAAAAACATTAAACCATCCTCAGGAGGGGACCTAGAAATTACAACAC** ICAGTTTATGGGATCAAAGCCTAAAGCCATGTGTAAAGTTGACCCCACTCTGTGTCACTTTAAATTGTACAGAGGT ATACCTCAGCCCTAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAA TTCCTATACATTATTGTGCTCCAGCTGGT ATAGCTTTAATTGTAGAGGAGAATTTTTCTATTGCAATACATCGGGCCTGTTTAGTATAAATTATACAGAAAATAA AGGAAGCACAAATGATAGCACAAATAATAACACAGAGATATTCAGACCTGCAGGAGGAGATATGAGGACAATT TAATGTTACCAGAAATGTTAATAATAGCGTGGTTAATAATACCACAAATGTTAATAATAGCATGAATGGAGACAT TATGCGATTCTAAAGTGTAATAATAAGACATTCAATGGGACAGGACCATGCCATAATGTCAGCACAGTACAATGT <u>AGACCCAACAATAATACAAGACAAAGTATAAGAATAGGACCAGGACAAACATTCTATGCAACAGGAGACATAAT</u> AATGTACGCCCCTCCCATTGAAGGAAACATAGCATGTAAATCAGATATCACAGGGCTACTATTGGTTCGGGATGG GGAGGAGTGAATTGTATAAGTATAAAGTGGTAGAAATTAAGCCATTGGGAATAGCACCCACTGAGGCAAAAAGG ACACATGGAATTAAGCCAGTGGTATCAACTCAACTACTGTTAAATGGTAGCCTAGCAGAAGAAGGGATAATAT <u> AGGAGACATAAGACAAGCACATTGTAACATTAGTAGGACTAACTGGACTAAGGCTTTACGAGAGGTAAGGAACA</u> AGAGTGGTGGAGTAA (SEQ ID NO:11)

Codon optimized gp120.Czm DNA sequence:

<u> AGCCTGTGGGACCAGAGCCTGAAGCCCTGCGTGAAGCTGACCCCCTGTGCGTGACCCTGAACTGCACCGAGGTGAACGT</u> CCCAGCAGCGGCGGCGACCTGGAGATCACCACCACCACTTCAACTGCCGCGGCGAGTTCTTCTACTGCAACACAGCGG GATCGTGCTGGGCAACGTGACCGAGAACTTCAACATGTGGAAGAACGACATGGTGGACCAGATGCACGAGGACATCATC CTGAACGAGACGACGGCAGGGAGACCGGCAACAGCAGCAAGTACTACCGCCTGATCAACTGCAACACCAGCGCCCTGA CGCATCGGCCCCGGCCAGACCTTCTACGCCACCGGCGACATCATCGGCGACATCCGCCAGGCCCACTGCAACATCAGCCG GACCCGCAACGTGAACAACAGCGTGGTGAACAACACCCCAACGTGAACAACAGCATGAACGGCGACATGAAGAACTG CAGCTTCAACATCACCACCGAGCTGAAGGACAAGAAGAAGAACGTGTACGCCCTGTTCTACAAGCTGGACATCGTGAGC AACAACAAGACCTTCAACGGCACCGGCCCCTGCCACAACGTGAGCACCGTGCAGTGCACCCACGGCATCAAGCCCGTGG <u> IGAGCACCCAGCTGCTGATGGCAGCCTGGCCGAGGAGGGCATCATCATCCGCAGCGAGAGAACCTGACCAACAACGT</u> CACCAACTGGACCAAGACCCTGCGCGAGGTGCGCAACAAGCTGCGCGAGCACTTCCCCCAACAAGAACATCACCTTCAAG CCTGTTCAGCATCAACTACACCGAGAACAACACCGACGGCACCCCCATCACCCTGCCCTGCCGCATCCGCCAGATCATCA 4 CATGTGGCAGGAGGTGGGCCGCGCGCCATGTACGCCCCCCCATCGAGGGCAACATCGCTGCAAGAGAGGCACATCACCGG CCAGGCCTGCCCCAAGGTGAGCTTCGACCCCATCCCCATCCACTACTGCGCCCCCGGCGGCTACGCCATCCTGAAGTGC TGGGGCAACCTGTGGGTGACCGTGTACTACGGCGTGCCCGTGTGGAAGGAGGGCCAAGACCACCCTGTTCTGCGCCAGCG AGGCCAAGCGCCGCGTGGTGGAGCGCGAGAAGCGCTGA (SEQ ID NO:12)

Wild type gp120.E DNA sequence

GATATAGTACAAATTAATAGTAGTGAGTATAGGTTAAATTGTAATACTTCAGTCATTAAGCAGGCTTGTCAAA <u> AGTITTATGGGATCAAAGTCTAAAGCCATGTGTAAAGTTAACTCCTCTCTGCGTTACTTTGACTTGTACCATGCTACT</u> <u>AACAAAATGGAATGAAGCTTTAAAACAGGTAGCTGGGAAATTAAAAGAACACTTTAATAAGACAATAATCTTTCAA</u> MGTGGGTCACAGTCTATTATGGGGTACCTGTGTGGAAAGATGCAGATACCACCCTATTTTGTGCATCAGATGCCAA 4 GCACATGAGACAGAAGTGCACAATGTCTGGGCCACACATGCCTGTGTACCCACAGACCCCAACCCAAGAAATA CTGAATTGTACCAATTTGACCAATGGCAATAAGACAACTAATGTCTCTAACATAATAGGAAATCTAACAGATGAAG IAAGAAACTGTTCTTTCATATGACCACAGAACTAAGAGATAAGAAGCAGAAGGTCTATGCACTTTTTTATAAGCTT CAATGGGACAGGGCCATGTAAAAATGTCAGCTCAGTACAATGCACACATGGAATTAAGCCAGTGGTATCAACTCAA AGGACCAGGACAAGTATTCTATAGAACAGGAGACATAAACAGGAGATATAAAGAAAAGCATATTGTGAGATTAATGA CCACCCTCAGGAGGAGATCTAGAAATTACAATGCATCATTTTAAATTGTAGAGGGGAATTTTTCTATTGCGATACAAC GCAAATTGTAAACATGTGGCAGGGAGCAGGGCAAGCAATGTATGCTCCTCCCATCAGTGGAATAATTAAGTGTGTA | ICAAATATTACAGGAATACTATTGACAAGAGATGGTGGTGCTAATAATTCGGCTAGTGAGACCTTCAGAGACCTTGGAG GATATCCTTTGATCCAATTCCTATACATTATTGTACTCCAGCTGGTTATGCGATTTTAAAGTGTAATGATAAGAATTT GAGGAAATATAAAGGACAATTGGAGAAGTGAATTATATAAATATAAAGTAGTACAAATTGAACCACTAGGAATAG CACCTGGAAAATGTAACAGAAAATTTTAACATGTGGAAAAATAAAATGGTAGAGAGATGCAGGAGGATGTAAATC FAATAGTGCACCTTAATAAATCTGTAGAAATCAGTTGTACCAGACCCTCCACCAATACAAGAACAAGTATACGTAT ACAACTGTTTAATAGAACTTGGGGAGAAAATGAAACCAGAGGGGGGGTAATATCACACTTCCATGCAAGATAAA CACCCACCAGGGCAAAGAGAAGAGTGGTGGAGTAA (SEQ ID NO:13)

Codon optimized gp120.E DNA sequence:

CAGCTTCCACATGACCACCGAGCTGCGCGACAAGAAGCAGAAGGTGTACGCCCTGTTCTACAAGCTGGACATCGTGCAG ATCAACAGCAGCGAGTACCGCCTGATCAACTGCAACACCAGCGTGATCAAGCAGGCTGCCCCAAGATCAGGTTCGACC A CGA GACCCGCGAGGCCAGGAACATCACCCTGCCTGCAAGATCAAGCAGATCGTGAACATGTGGCAGGGAGCTGGCC CCACGAGACCGAGGTGCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCAGGAGATCCACCT GGGACCAGAGCCTGAAGCCCTGCGTGAAGCTGACCCCCTGTGCGTGACCCTGACCTGCACCAACGCCACCCTGAACTG CACCAACCTGACCAACGGCAACAAGACCACCACGTGAGCAACATCATCGGCAACCTGACCGACGAGGGGCAACTG GAGCGTGGAGATCAGCTGCACTCGCCCCAGCACCAACACCCGCACCAGCATCCGCATCGGACCTGGCCAGGTGTTCTAC 2GCACCGGCGACATCACCGGCGACATCCGCAAGGCCTACTGCGAGATCAACGAGACCAAGTGGAACGAGGCCCTGAAG **a**GGCCATGTACGCCCCACCATCAGCGGCATCATCAAGTGCGTGAGCAACATCACGGCATCCTGCTGACCGGCACGG CAAGTACAAGGTGGTGCAGATCGAGCCCCTGGGCATCGCCCCCCACTCGCCCCAAGCGCCCGCGTGGTGGAGTAA (SEQ ID CCATCCCCATCCACTACTGCACCCCTGCTGGCTACGCCATCCTGAAGTGCAACGACAAGAACTTCAACGGCACCGGACC CCTGGCCGAGGAGGAGATCATCATCAGCAGCGAGAACCTGACCAACAACAACGCCAAGACCATCATCGTGCACCTGAACAA ACCATGCACCACTTCAACTGCAGAGGCGAGTTCTTCTACTGCGACACCCCCAGCTGTTCAACCGCACCTGGGGGCGAGA CTGCAAGAACGTGAGCAGCGTGCAGTGCACCCACGGCATCAAGCCCGTGGTGAGCACCCCAGCTGCTGCTGAACGGCAG CAGGTGGCCGGCAAGCTGAAGGAGCACTTCAACAAGACCATCATCTTCCAGCCTCCCAGCGGAGGCGACCTGGAGATC GGAGAACGTGACCGAGAACTTCAACATGTGGAAGAACAAGATGGTGGAGCAGATGCAGGAGGAGGACGTGATCAGCCTGT

Wild type gp120.A DNA sequence:

ATGCATACAGATATAATCAGTCTATGGGACCAAAGCCTAAAACCATGTGTACAGTTAAACCCCTCTCTGCGT TACTITAGATIGIAGCTATAACATCACCAATAATATCACCAATAGCATCACCAATAGCTCAGTTAACATGA ITAACGAGACTGTAACAATTAATTGTACCAGACCTAACAACAATACAAGAAAAAGTGTACGTATAGGACC GTCACAATGGAATAGAGCTTTACACCAGGTAGTTGGACAATTAAGAGAATACTGGAACACAAAAATC ITTAAAAACTCCTCAGGAGGGGATTTAGAAATTACAACACATAGTTTTAATTGTGGAGGAGAATTTTTTA GCCCCTCCCATTCAAGGAGTAATAAGGTGTGAATCAAACATTACAGGACTAATATTAACAAGAGATGGTG ITGTGGGTCACAGTCTATTATGGGGTACCTGTGTGGAAAGATGCAGAGACTACCTTATTTTGTGCATCAGA IGCGAAAGCATATGATACAGAAGTGCATAATGTCTGGGCTACGCATGCCTGTGTGTACCTACAGACCCCAAC CCACAAGAAATATATGGAAAATGTGACAGAAGAGTTTAACATGTGGAAAAATAACATGGTAGAGCAG CACTITITITATAAACTTGATGTAGAAATTAATAATGGTAATAACAGTAGTAATCTGTATAGATTAATA IGCCCCAGCTGGTTATGCGATTCTAAAATGTAATGATAAGGAGTTCAATGGAACAGGGCTATGCAAAAAT GGGGTAACATCAATGAAAGTCAAATCTTCAGACCTGGAGGAGAGATATGAGGGACAATTGGAAGAGTG <u> AATTGTAATACCTCAGCCCTTACACAGGCTTGTCCAAAGGTAACCTTTGAGCCAATTCCCATACGTTATTG</u> TTGTAATACATCAGGCCTGTTTAATAGTAATTGGACACATAATGACACTGCCAGCATGAAACCAAATGAC GTCAGCACAGTGCAATGCACACATGGAATCAGGCCAGTAGTATCAACTCAACTGCTGTTAAATGGCAGTT GAGAAGAAATAAAAAACTGCTCTTTCAATATGACCACAGAATTAAGGGATAAGAATCGGAAGGTATATT AGGACAAACATTCTATGCAACAGGTGATATAATAGGGGATATAAGACAAGCACATTGTAATGTCAGTGG **FGGTGGAGTAA** (SEQ ID NO:15)

Codon optimized gp120.A DNA sequence:

<u> 3AGCCTGAAGCCCTGCGTGCAGCTGACCCCCCTGTGCGTGACCCTGGACTGCAGCTACAACATCACCAACAACATCACCAAC</u> CTGCCGCATCAAGCAGATCATCAACATGTGGCAGCGCGTGGGCCAGGCCATCTACGCCCCTCCCATCCAGGGCGTGATCCG <u> SGGGGGGGACATGCGCGACAACTGGCGCAGCGAGCTGTACAAGTACAAGTGGTGGTGCGCATCGAGCCCCTGGGCGTGGCCCC</u> GCCCACTGCAACGTGAGCGGCAGCCAGTGGAACCGCGCCCTGCACCAGGTGGTGGGCCAGCTGCGCGAGTACTGGAACACC <u> ACCATCATCTTCAAGAACAGCAGCGGCGGCGACCTGGAGATCACCACCACAGCTTCAACTGCGGCGGCGGGGTTCTTCTACT</u> <u> 3AACCGCAAGGTGTACAGCCTGTTCTACAAGCTGGACGTGGTGCAGATCAACAACAGGGCAACAACAGCAGCAGCAACCTGTACCG</u> CCGCCGGCTACGCCATCCTGAAGTGCAACGACAAGGAGTTCAACGGCACCGGCCTGTGCAAGAACATGAGCACCGTGCAG GCAACACCAGCGGCCTGTTCAACAGCAACTGGACCCACAACGACGCCCAGCATGAAGCCCAACGACACCATCACCCTGC CTGCGAGAGCAACATCACCGGCCTGATCCTGACCCGCGACGCGGCGGCAACATCAACGAGAGGCAGATCTTCCGCCCGG <u> IACGACACCGAGGTGCACAACGTGTGGGCCACCCACGCCTGCGTGCCCACCGACCCCAACCCCCAGGAGATCTACATGGAG</u> CTGATCAACTGCAACACCAGCGCCCTGACCCAGGCCTGCCCCAAGGTGACCTTCGAGCCCATCCCCATCCGCTACTGCGCC IGCACCCACGGCATCCGCCCCGTGGTGAGCACCCAGCTGCTGCTGAACGGCAGCCTGGCCGAGGGCAAGGTGATGATCCGC AACAACACCCGCAAGAGCGTGCGCATCGGCCCCGGCCAGACCTTCTACGCCACCGGCGACATCATCGGCGACATCATCCGCCAG CTGTGGGTGACCGTGTACTACGGCGTGCCCGTGTGGAAGGACGCCGAGACCACCCTGTTCTGCGCCAGCGACGCCAAGGCC 4 GCATCACCAACAGCGCGGAACATGCGCGAGGAGATCAAGAACTGCAGCTTCAACATGACCACCGAGCTGCGCGACAAA CACCAAGGCCAAGCGCCGCGTGGTGGAGTAA (SEQ ID NO:16)

FIG. 38

7 11. 7